CRF AND DOPAMINE INTERACTIONS. A. F. Schatzberg, MD,[a] J. Posener, MD[b], D. C. Lyons, PhD,[a] S. Levine, PhD,[a]
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Considerable data have emerged that patients with delusional major depression are characterized by marked increases in activity of the hypothalamic-pituitary-adrenal (HPA) axis and dopamine systems. Our group has been exploring interactions between the two systems, emphasizing the effects the HPA axis may exert on brain dopamine. In this talk, we review data from a series of studies in man and the squirrel monkey.

A number of years ago, our group and others reported that the administration of dexamethasone to healthy controls results in significant elevations in plasma dopamine (DA) or homovanillic acid (HVA) levels. These increases occur some 17 hours post administration and persist for at least 17-24 hours. Similarly, we and others have reported that in the rat administration of dexamethasone or corticosterone results in significant increases in DA turnover in mesolimbic brain regions. In this presentation, we report on a study in which 10 healthy controls were challenged sequentially with hydrocortisone, o-CRH, ACTH, or saline under double blind, random assignment conditions. Data indicate that challenge of the axis with all 3 substances results in significant, delayed elevations of plasma HVA levels. The implications of these data are discussed.

In the squirrel monkey, separation from triadic groups results in an initial increase in circulating ACTH and cortisol levels. The increase in ACTH is reversed within 24 hrs. whereas the elevations in cortisol persist for at least 2 weeks. Plasma HVA levels are increased by day 3 and these levels remain increased for at least 2 weeks. When monkeys are characterized into high and low cortisol responders, plasma HVA is significantly higher throughout the separation in the high cortisol group than in the low cortisol group. Moreover, these animals continue to demonstrate elevated plasma HVA levels after they are placed back into groups even though their cortisol levels normalize. The possible role CRH plays in mediating this response is discussed as are the potential clinical implications.